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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/825,688	04/16/2004	Hartmut Vodermaier	0652.2610001/EKS/VSR	8679

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EXAMINER	
WOOD, AMANDA P	
ART UNIT	PAPER NUMBER
1657	

DATE MAILED: 10/11/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/825,688	VODERMAIER ET AL.	
	Examiner	Art Unit	
	Amanda P. Wood	1655	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,5 and 7-9* is/are rejected.

7)☒ Claim(s) *4 and 6* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Objections

Claims 4 and 6 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 3 and 5 recite the limitation "the C-terminal peptide" in line 1. There is insufficient antecedent basis for this limitation in the claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-3, 5, and 7-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gmachl et al (US 2002/0028472 A1) in view of Prinz et al (Current Biology 1998).

A method for determining whether a test compound has the ability to specifically inhibit the APC is claimed.

Gmachl et al beneficially teach screening methods for identifying compounds that inhibit the APC. In particular, Gmachl et al teach that to initiate sister chromatid separation, the APC has to ubiquitinate the anaphase inhibitor Securin, whereas exit from mitosis requires the APC-mediated ubiquitination of B-type cyclins, a reaction which depends on activation of the APC by CDC20 and CDH1. Gmachl et al further teach that CDC20 and CDH1 transiently associate with the APC at the end of mitosis and in G1, respectively. Gmachl et al beneficially teach that the APC has been suggested as a target for chemotherapeutic intervention because the activity of the APC is essential for sister chromatid separation and for exit from mitosis during cell proliferation, and interfering with this function would prevent tumor cells from completing mitosis. Furthermore, Gmachl et al teach that tumor cells might be especially sensitive to drugs that interfere with APC function because they undergo anaphase in the presence of chromosomal damage that would prevent activation of the APC in normal cells. Gmachl et al teach a method wherein compounds are tested for the ability to inhibit the APC's ability to ubiquitinate Securin, which initiates sister chromatid separation. Gmachl et al teach a method wherein FRET is used to determine whether compounds inhibit the above ubiquitination reaction in the presence and absence of a

test compound. Furthermore, Gmachl et al beneficially teach a secondary assay wherein an APC with the ability to ubquitinate APC substrate protein in a strictly regulated manner (e.g., the regulation depending on binding to regulatory proteins like CDH1 and CDC20), is employed, such as holo APC or APC3/CDC27, as taught by Kramer et al (Current Biology 1998). Gmachl et al beneficially teach that the compounds identified by these assay methods function as APC inhibitors and are expected to arrest cells in metaphase of mitosis, subsequently inducing apoptotic cell death (see, for example, pg. 1, pgh. [0006]; pg. 4, pgh. [0045-0048]; pg. 5; pg. 6, pgh [0067]; and pg. 8, pgh. [0082]).

Gmachl et al do not expressly teach a method wherein a compound is tested for its ability to interfere with binding of CDH1 or CDC20 to the APC or one or more fragments, wherein the APC or one or more fragments is APC3 or APC7 or a fragment thereof.

Prinz et al beneficially teach that CDH1 and CDC20 are substrate-specific regulators of APC-dependent proteolysis. In particular, Prinz et al teach that levels of CDH1 protein are constant throughout the cell cycle, whereas CDC20 RNA and protein are present only during late S phase and mitosis, and CDC20 protein is unstable throughout the entire cell cycle. Furthermore, Prinz et al beneficially teach that this instability depends on CDC23 and CDC27 (i.e., APC3), which encode subunits of the APC (i.e., to which CDC20 would bind) (see, for example, Abstract, pg. 751, pg. 755, and pg. 756).

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the methods disclosed by Gmachl et al based upon the beneficial teachings provided by Prinz et al with respect to the teaching that CDC20 asscociates with CDC27 (i.e., APC3), as discussed above. Furthermore, Gmachl et al particularly point out that the APC depends on activation by CDC20 and CDH1 for exit from mitosis and that it would be beneficial to explore for compounds that can inhibit the APC so to provide drugs that prevent tumor cells from completing mitosis. In particular, it would have been both obvious and beneficial for the skilled artisan to screen compounds for the ability to interfere with binding of CDC20 or CDH1 to APC, in lieu of screening compounds for the ability to inhibit the APC11-mediated ubiquitination reaction (i.e., screening for compounds to inhibit the reaction to exit mitosis as opposed to inhibit the reaction which initiates sister chromatid separation), based upon the beneficial teachings provided by Gmachl et al, that, in particular, interfering with the exit from mitosis could prevent tumor cells from completing mitosis, and is therefore, a particularly useful target for chemotherapeutic intervention. In addition, based upon the beneficial teachings provided by Gmachl et al with respect to assaying for compounds which inhibit the APC, specifically the secondary assay screening using a holo APC which interacts with CDC20 and CDH1, it would have been both obvious and beneficial for one of ordinary skill in the art at the time the claimed invention was made to provide an assay which test compounds for their ability to interfere with binding of CDH1 or CDC20 to the APC (or fragments thereof) by combining and APC that binds CDC20 or CDH1 (as taught by Gmachl et al) in the

presence and absence of a test compound with a peptide with the ability to interfere with binding of CDC20 or CDH1 to the APC, and determining whether the compound competes for binding, and then screening the compound for the ability to interfere with the activation of the APC by CDH1 or CDC20. Furthermore, based upon Applicant's admitted state of the prior art (see, for example, paragraph [0045] of pre-grant publication of the instant application), with respect to the subject matter of instant claim 7, it would have been obvious to one of ordinary skill in the art to use the well-known method of fluorescence polarization assays to assess the ability of the compounds to interfere with binding of CDH1 or CDC20 to the APC. The result-effective adjustment of particular conventional working conditions (e.g., using a APC fragment and/or particular fragment of CDC20 or CDH1) is deemed merely a matter of judicious selection and routine optimization which is well within the purview of the skilled artisan.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole, was *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made, as evidenced by the cited references, especially in the absence of evidence to the contrary.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amanda P. Wood whose telephone number is (571) 272-8141. The examiner can normally be reached on M-F 8:30AM -5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Terry McKelvey can be reached on (571) 272-0775. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

APW
Examiner
Art Unit 1655

APW

CHRISTOPHER R. TATE
PRIMARY EXAMINER